

## PATENT COOPERATION TREATY

REC'D 16 AUG 2005

WIPO


PCT

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PC32332A	<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/IB2004/002380	International filing date (day/month/year) 13.07.2004	Priority date (day/month/year) 25.07.2003	
International Patent Classification (IPC) or national classification and IPC C07D409/12, A61P11/00, A61P37/00, A61K31/4436, C07D409/14, C07D471/04, C07D417/14, C07D413/14			
Applicant PFIZER LIMITED et al			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the International application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand  09.08.2004		Date of completion of this report  18.08.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized Officer  Bosma, P  Telephone No. +31 70 340-	



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/IB2004/002380

---

**Box No. I Basis of the report**

---

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

**Description, Pages**

1-104 as originally filed

**Claims, Numbers**

1-24 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/IB2004/002380

---

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

---

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
  - ☒ claims Nos. 18,19 with respect to IA  
because:
    - ☒ the said international application, or the said claims Nos. 18,19 relate to the following subject matter which does not require an international preliminary examination (specify):  
**see separate sheet**
  - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  - ☐ no international search report has been established for the said claims Nos.
  - ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
    - the written form ☐ has not been furnished
    - ☐ does not comply with the standard
    - the computer readable form ☐ has not been furnished
    - ☐ does not comply with the standard
  - ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
  - ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/B2004/002380

---

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

---

1. Statement

Novelty (N)	Yes: Claims	1-24
	No: Claims	
Inventive step (IS)	Yes: Claims	1-24
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-17,20-24
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

---

**Box No. VIII Certain observations on the international application**

---

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 18 and 19 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: WO 01/57036 A (MARFAT ANTHONY ;PFIZER PROD INC (US); CHAMBER ROBERT JAMES (US)) 9 August 2001 (2001-08-09)  
D2: DATABASE CHEMCATS Chemical Abstracts Service, Columbus, Ohio, USA; XP002253965

**Novelty and Inventive step**

The document D1 is regarded as being the closest prior art to the subject-matter of claims 1-22 and 24, and has been acknowledged in the description. D1 also describes nicotinamide derivatives useful as PDE4 inhibitors.

The present compounds differ structurally very much from the ones of this known document D1 (eg a benzofused-heterocyclyl moiety in D1 in stead of the tetrahydro-thiopyran-4-yl moiety of the present invention) and are therefore novel.

The intermediates according to claim 23 were not found in the available prior art documents. D2 discloses a compound which is structurally different in the group R<sup>2</sup>. Therefore novelty is recognised for these intermediates.

The subject-matter of claims 1-24 (compounds, their pharmaceutical use, processes for their preparation, and intermediates) is consequently new (Article 33(2) PCT).

The problem to be solved by the present invention may be regarded as the provision of further compounds which can be used as PDE4 inhibitors.

The solution to this problem proposed in the present claims is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

From the prior art documents there were no incentives for replacing a benzofused-heterocyclyl moiety as known from D1 by the tetrahydro-thiopyran-4-yl moiety of the present invention. Moreover the present moiety R<sup>2</sup> has a specific meaning unknown from the available prior art documents.

The intermediates of claim 23 contribute to the structural differentiation of the end-products over the state of the art D1 and D2 and an inventive step can be recognised for this claim 23 as well.

### **Industrial applicability**

The present compounds are useful as PDE4 inhibitors.

For the assessment of the present claims 18 and 19 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

### **Re Item VIII**

#### **Certain observations on the international application**

Claims 8-10 contain references to the examples in the description. According to Rule 6.2(a) PCT, claims should not contain such references except where absolutely necessary, which is not the case here.

Claim 11 comprises all the features of claim 1 and is therefore not appropriately formulated as a claim dependent on the latter (Rule 6.4 PCT).